Gs G protein-coupled receptor signaling in osteoblasts elicits age-dependent effects on bone formation.

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Authors: Edward C Hsiao, Benjamin M Boudignon, Bernard P Halloran, Robert A Nissenson, Bruce R Conklin

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Public Summary:

Scientific Abstract:
Age-dependent changes in skeletal growth are important for regulating skeletal expansion and determining peak bone mass. However, how G protein-coupled receptors (GPCRs) regulate these changes is poorly understood. Previously, we described a mouse model expressing Rs1, an engineered receptor with high basal G(s) activity. Rs1 expression in osteoblasts induced a dramatic age-dependent increase in trabecular bone with features resembling fibrous dysplasia. To further investigate how activation of the G(s)-GPCR pathway affects bone formation at different ages, we used the tetracycline-inducible system in the Coll(2.3)(+)/Rs1(+) mouse model to control the timing of Rs1 expression. We found that the Rs1 phenotype developed rapidly between postnatal days 4 and 6, that delayed Rs1 expression resulted in attenuation of the Rs1 phenotype, and that the Rs1-induced bone growth and deformities were markedly reversed when Rs1 expression was suppressed in adult mice. These findings suggest a distinct window of increased osteoblast responsiveness to G(s) signaling during the early postnatal period. In addition, adult bones encode information about their normal shape and structure independently from mechanisms regulating bone expansion. Finally, our model provides a powerful tool for investigating the effects of continuous G(s)-GPCR signaling on dynamic bone growth and remodeling.